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PATENT

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SECOND REQUEST FOR CORRECTED FILING RECEIPT
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TO: OFFICE OF INITIAL PATENT EXAMINATION'S
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FAX NO.: 703-746-9195

RE: APPLICATION NO: 09/806,440

ART UNIT: 2642

INVENTORS: Miele et al.

ATTY REF.: 4239-58051

FILED: March 30, 2001

TITLE: APOPTOSIS INDUCING AGENTS AND METHODS


Assistant Commissioner For Patents
Washington, D.C. 20231

An error appears on the official Filing Receipt issued for the above-identified patent application. In particular, two U.S. provisional applications are omitted from the priority data listed on the official Filing Receipt. Attached hereto is a copy of the official Filing Receipt (Exhibit A) with the requested correction shown thereon. Also attached is a copy of the cover page of the published PCT application (Exhibit B), showing the priority claim. Also attached is a copy of the Combined Declaration and Power of Attorney for Patent Application (Exhibit C) showing the priority claim.

A Request for Corrected Filing Receipt was faxed to the U.S. Patent and Trademark Office on April 25, 2002, but to date a Corrected Filing Receipt has not been received.

Please correct the identified error and issue a corrected official Filing Receipt.

I hereby certify that this paper and the associated documents are being facsimile transmitted to the U.S. Patent and Trademark Office on the date shown below.


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APPLICATION NUMBER	FILING DATE	GRP ART UNIT	FIL FEE REC'D	ATTY DOCKET NO	DRAWINGS	TOT CLAIMS	IND CLAIMS
09/806,440	03/30/2001	1646	2642	4239-58051	14	79	12

CONFIRMATION NO. 1318

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Receipt is acknowledged of this nonprovisional Patent Application. It will be considered in its order and you will be notified as to the results of the examination. Be sure to provide the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION when inquiring about this application. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. If an error is noted on this Filing Receipt, please write to the Office of Initial Patent Examination's Customer Service Center. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections (if appropriate).

Applicant(s)

Lucio Miele, Morningside, IL;
Leslie S. Shields, Encinitas, CA;
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Domestic Priority data as claimed by applicant

THIS APPLICATION IS A 371 OF PCT/US99/23162 10/01/1999
WHICH CLAIMS BENEFIT OF 60/102,816 10/02/98, AND
60/124,119 03/12/99

Foreign Applications

Add

Projected Publication Date: Not Applicable, filed prior to November 29, 2000

Non-Publication Request: No

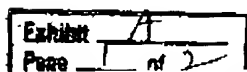
Early Publication Request: No

Title

Methods and compositions for inducing differentiation and apoptosis in cells tha overexpress the notch protein

Preliminary Class

435



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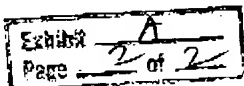
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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7: C12N 15/11, A61K 39/395, 31/16, C07K 16/28, C12N 5/20, G01N 33/574, 33/577, A61K 31/475, 31/337, A61P 35/00 // C12N 5/06, 5/08, (A61K 39/395, 31:16) (A61K 39/395, 31:475) (A61K 39/395, 31:337)		A2	(11) International Publication Number: WO 00/20576 (43) International Publication Date: 13 April 2000 (13.04.00)
(21) International Application Number: PCT/US99/23162 (22) International Filing Date: 1 October 1999 (01.10.99)		(74) Agent: NOONAN, William, D., M., D., Klarquist, Sparkman, Campbell, Leigh & Whinston, LLP, One World Trade Center, Suite 1600, 121 S.W. Salmon Street, Portland, OR 97204 (US).	
(30) Priority Data: 60/102,816 2 October 1998 (02.10.98) US 60/124,119 12 March 1999 (12.03.99) US		(71) Applicant (for all designated States except US): THE GOVERNMENT OF THE UNITED STATES OF AMERICA, as represented by THE SECRETARY, DEPT. OF HEALTH AND HUMAN SERVICES, THE NATIONAL INSTITUTES OF HEALTH [US/US]: Office of Technology Transfer, Suite #325, 6011 Executive Boulevard, Rockville, MD 20852 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): MIELE, Lucio [IT/US]; 2N771 Morningside Avenue, West Chicago, IL 60185 (US); SHIELDS, Leslie, S. [CA/US]; 8507 Capricorn Way #80, San Diego, CA 92126 (US). FUCHS, Chana [US/US]; 4450 S. Park Avenue #1106, Chevy Chase, MD 20815 (US).	
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Published Without international search report and to be republished upon receipt of that report.			

(54) Title: APOPTOSIS INDUCING AGENTS AND METHODS

(57) Abstract

Methods and compositions are disclosed for inducing differentiation and apoptosis in cells that overexpress Notch proteins. A cell fate determining function of Notch is specifically disrupted at a time when the cell is undergoing differentiation, which causes the cell to undergo apoptosis. The invention includes therapies for tumors that overexpress a Notch protein (such as Notch-1) by inducing differentiation of the cells in the tumor with a differentiation inducing agent, such as HMBA, in combination with an agent that disrupts the function of the Notch protein. At a time during which differentiation has been promoted, and the cell is susceptible to interference with the anti-apoptosis effect of Notch, the function of the Notch protein is disrupted. Disruption of Notch function can be achieved, for example, by a differentiation inducing agent such as HMBA, combined with antibodies that specifically bind to Notch and inactivate it, for example a monoclonal antibody that recognizes Notch-1 EGF-like repeats 11 and 12, such as monoclonal antibodies A6, C11 or F3. Disruption of Notch function can also be achieved by the expression of antisense oligonucleotides that specifically interfere with expression of the Notch protein on the cell, alone or in combination with antineoplastic agents.

Exhibit B
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